Journal of Current Chemical & Pharmaceutical Sciences

J. Curr. Chem. Pharm. Sc.: 1(1), 2011, 15-18

A SIMPLE SPECTROPHOTOMETRIC DETERMINATION OF VALACYCLOVIR IN PHARMACEUTICAL PREPARATIONS

G. SRIHARI, N. UMA MAHESWAR REDDY, N. RAMI REDDY* and I. E. CHAKRAVARTHI[a]

S. B. S. Y. M. Degree College, KURNOOL (A.P.) INDIA
[a]Rayalaseema University, KURNOOL (A.P.) INDIA

(*Received : 03.10.2011, Revised : 11.10.2011, Accepted : 12.10.2011*)

ABSTRACT

A simple, sensitive and economical spectrophotometric method has been developed for the estimation of valacyclovir in pharmaceutical dosage forms. The method is based on the formation of a orange red coloured azo product by the diazotization of valacyclovir followed by a coupling reaction with resorcinol. The absorbance of orange red coloured solution is measured at 440 nm against reagent blank. Beer's law is obeyed in the concentration of 50-250 µg/mL of valacyclovir. Statistical analysis proves that the proposed method is reproducible and selective for the estimation of valacyclovir in bulk drug and in its tablet dosage form.

Key words: Spectrophotometry, Valacyclovir, Resorcinol, Formulations.

INTRODUCTION

Valacyclovir chemically, *L*-valine-2-[(2-amino-1, 6-dihydro-6-oxo-9-hipurin-9-yl) methoxy] ethyl ester is the *L*-valyl ester prodrug of the antiviral drug acyclovir that exhibits activity against herpes simplex virus types, 1 (HSV-1) and 2 (HSV-2) and vericellazoster virus. The mechanism of action of acyclovir involves the highly selective inhibition of herpes virus DN Areplication, via enhanced uptake in herpes virus-infected cells and phosphorylation by viral thymidine kinase. The substrate specificity of acyclovir triphosphate for viral, rather than cellular, DNA polymerase contributes to the specificity of the drug. Valacyclovir is available as tablet dosage form in the market. Few spectrophotometrc methods[1-4], HPLC methods[5-11], RP-HPLC Method[12], are reported in the literature for the determination of valacyclovir in pharmaceutical formulations.

Spectrophotometry is the technique of choice even today in the laboratories of research, hospitals and pharmaceutical industries due to its low cost and inherent simplicity. This paper describes a simple rapid, simple, sensitive and economical spectrophotometeric method for the determination of valacyclovir in commercial dosage forms. In this method the amino group in valacyclovir is diazotized with sodium nitrite and hydrochloric acid at 0^0C temperature. After diazotization, the diazonium salt is coupled with resorcinol. The orange red coloured chromogen formed in the method is stable for more than 24 hours. The orange red coloured chromogen was measured at 440 nm against reagent blank prepared similar manner omitting drug

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Available online at www.sadgurupublications.com
*Author for correspondence; E-mail: ramireddy65@gmail.com; Ph.: 08518-273765

solution. Hence the author has made an attempt to develop simple and sensitive spectrophotometric methods for the estimation of valacyclovir in bulk drugs and in pharmaceutical formulations.

EXPERIMENTAL

Materials and methods

All absorbance measurements were made on a Spectronic 1001 plus spectrophotometer (Milton Roy Company, USA) with 1 cm matched quartz cells. All the solutions were freshly prepared. All solvents and other chemicals used through this study were of analytical grade. Double distilled water was used throughout the investigation. Hydrochloric acid (0.1 N) was prepared and standardized with standard procedure. Sodium nitrite (0.1 N) was prepared by dissolving 0.69 g in 100 mL distilled water. Sodium carbonate (0.5 N) was prepared by dissolving 5.3 g in 100 mL distilled water. Resorcinol (1%) and urea (1%) solution were prepared.

Preparation of standard solution

A standard stock solution containing 1 mg/mL was prepared by dissolving 50 mg of valacyclovir in 50 mL of methanol. From this, a working standard solution containing 100 µg/mL was prepared.

Assay procedures

Various aliquots (0.2, 0.4, 0.6, 0.8, 1.0 mL) of valacyclovir were transferred into a series of 10 mL volumetric flask. To each flask, 1.0 mL of 0.1 N hydrochloric acid and 1.0 mL of 0.1 N sodium nitrite solutions was added with swirling and kept aside for 5 min., at 0-50^{0}C temperature for complete diazotization. Then 1.0 mL of 1% urea solution was added in each flask and shaken frequently to allow nitrogen gas to escape. After 2 min. 1.0 mL of 0.5 N sodium carbonate solution and 1.0 mL of 1% resorcinol solution was added. The volume in each flask was adjusted to 10 mL with methanol. After 10 min., the absorbance of orange red coloured solution was measured at 440 nm against reagent blank prepared by similar manner omitting drug solution. The amount of valacyclovir was computed from calibration curve.

Pharmaceutical formulations

Twenty tablets containing valacyclovir were weighed and finely powdered. An accurately weighed portion of the powder equivalent to 50 mg of valacyclovir was dissolved in a 25 mL of methanol and mixed for about 5 minutes and then filtered. Then the volume was diluted to 50 mL with methanol and analyzed as given under the assay procedures for bulk samples. The results are represented in Table 2.

Recovery Studies

To ensure the accuracy and reproducibility of the results obtained, known amounts of pure drug was added to the previously analysed formulated samples and these samples were reanalyzed by the proposed methods and also performed recovery experiments. The percentage recoveries thus obtained were given in Table 2.

RESULTS AND DISCUSSION

In this method valacyclovir underwent diazotization when treated with sodium nitrite and hydrochloric acid. The excess nitrous acid during the diazotization could be removed by the addition of urea solution. The solution was shaken frequently to allow the nitrogen to escape. For the diazotization process, valacyclovir readily diazotized in acidic medium and that the diazonium cation would then react with a

coupling reagent of resorcinol to produced an orange red coloured azo product. This orange red colour shows maximum absorbance at 440 nm. The absorption spectra of orange red coloured azo product was shown in Fig. 1. The colorless reagent blanks under similar conditions showed no absorption. The optimum conditions were established by varying one parameter at a time and keeping the others fixed and observing the effect on absorbance of chromogen for the proposed method**.** Statistical analysis was carried out and the results were found to be satisfactory. Recovery studies were close to 100% that indicates good accuracy of the methods. The optical characteristics such as absorption maxima, Beer´s law limits, molar absorptivity and Sandell´s sensitivity are presented in Table 1.

Table 1: Optical characteristics of proposed method

Parameters	Proposed method
λ_{max} (nm)	440
Beer's law limit (µg/mL)	50-250
Molar absorptivity (L mole^{-1} cm^{-1})	1.2 x 10^3
Sandell's sensitivity (µg cm^{-2} / 0.001 absorbance unit)	0.123
Regression equation (Y = a + bX)	Y = 0.0078 X + 0.016
Slope (b)	0.0078
Intercept (a)	0.016
Correlation coefficient (r)	0.9993

*Y = a + b X, where Y is the absorbance and X concentration in µg/mL

A = Intercept

B = Slope

The regression analysis using method of least squares was made for the slope (b), intercept (a) and correlation (r) obtained from different concentrations and results are summarized. The high molar absorptivities of the resulting colored complexe indicate the high sensitivity of the method. The percent relative standard deviation, standard deviation and student's 't' test values calculated from the five measurements of valacyclovir are presented in Table 2. Relative standard deviation values and standard deviation were low that indicates the reproducibility of the proposed methods. In the student's 't' tests, no significant differences were found between the calculated and theoretical values of the proposed method at 95% confidence level. This indicated similar precision and accuracy in the analysis of valacyclovir in its tablets. The commonly used additives such as starch, lactose, titanium dioxide, and magnesium stearate do not interfere with the assay procedures.

Table 2: Assay of Valacyclovir in tablets

S. No.	Tablets (mg)	*Amount Found (mg) ± S.D*	% Recovery	% RSD*	*t_{cal}
1	500	500.1 ± 0.032	100.06	0.0654	0.6830
2	500	500.03 ± 0.017	99.98	0.0351	0.3816

*Average of five determination based on the label claim

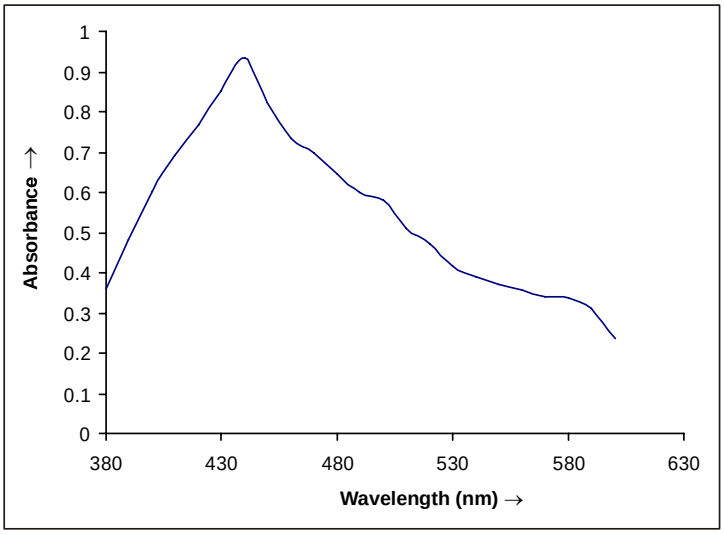

Fig. 1: Absorption spectrum of diazotized valacyclovir coupled with resorcinol at 440 nm

CONCLUSION

The proposed methods make use of simple reagents, which an ordinary analytical laboratory can afford. The proposed methods can be used for the routine quality control analysis of valacyclovir in industry, research laboratories and hospitals.

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